

Nutrition Reviews

Volume 42

March 1984

Number 3

Tenth Annual Marabou Symposium

"Food Sensitivity"

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Opening Address

by Håkan Mogren

Ladies and Gentlemen,

You are all very welcome to this Marabou symposium on Food Sensitivity. This year we celebrate the 10th anniversary of the Marabou symposia. Discussion of nutrition subjects by the public frequently consists of opinions and prejudices, but not very often of facts. We in the food industry have not always known how to get the proper facts to present to public discussions. Many fields are new and unexplored, and progress so rapid, that it has been difficult to get to the state of the art in a specific subject. In our company, we also have occasionally been unclear about the role of non-essential nutrients such as sucrose in modern nutrition.

That was the case ten years ago when my predecessor as president of Marabou, Johan Throne-Holst, together with our consultant, Professor Fredrick J. Stare, thought it might be a good idea to arrange a symposium with the very best specialists of the field of sugar in nutrition to obtain a proper picture of the situation. The first symposium turned out so well that we decided to go on to cover another very important subject: Nutritional Improvement of Foods. And so we were on the way.

The meetings are planned by an advisory group of the company. The main influence of the company as the organizer has been to make sure that the selected subject is of interest and practical application to the food industry. As soon as the subject has been chosen we add to the committee specialists of the field in question. The goal for the committee has then been to get the very best speakers and discussants of the subject. We are most proud and

happy to have always managed to get those we wanted and to have the proceedings of the symposia well received all over the world. It has been of great help that the proceedings have been published in the Swedish *Näringsforskning* as well as in *Nutrition Reviews*.

We are determined to keep the form of these symposia unique. This means short speeches, lots of time for discussions and time for informal get-togethers. We want you scientists to meet and to formulate the state of the art for the subject chosen. As you know, it is not always easy to get scientists to adopt the same view in summarizing a meeting. We think that the way to solve that is to use what I call the "pope election method." That means we put the participants together and do not let them out until we have seen the white smoke that they have agreed. So every year we have made a boat trip on Sunday and so far we have never failed in agreeing upon the summary statement before the boat lands. I am hopeful that this method will work also this year.

You might ask what does Marabou as a company get out of these symposia. Well, as I told you, we get the latest information on the specific subject of each symposium which otherwise we would have to research ourselves. Secondly, we get very good contacts, both professional and personal, with outstanding members of the scientific community. Thirdly, it has given us a platform for discussions with authorities. Our intention has never been to get deeply involved in nutritional science ourselves, but we are a food company, we do some research and we enjoy presenting our views to the best in the nutrition field. Finally, it has contributed to an international reputation for the company. Many people don't know what kind of business we are in. Some believe that Marabou is a city in

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the north of Europe. So far it isn't.

In summary, we have enjoyed very much these meetings, and the opportunity to meet all of you competent and fine people. We have made many good friends, and that is important in life.

Another activity in the field of nutrition connected with Marabou is the Henning and Johan Throne-Holst Foundation of Scientific Research. According to the board of the Foundation, the interest on the funds should go to scholarships in nutrition. Preferably awards should be given to young Swedish scientists for research projects abroad at leading institutes. As the chairman of the foundation I have the pleasure to announce that the scholarships this year will go to:

- Doctor Olle Hernell, 130,000 Swedish Crowns, for studies at the Brigham and Women's Hospital, Boston, USA, regarding "effect of the lipase of human milk on dietary lipids during digestion and on fat absorption."

- Doctor Sten Jameson, 100,000 Swedish Crowns, for studies at the University of California, Davis, USA, regarding "resorption of trace elements during pregnancy."

- Doctor Antal Nemeth, 60,000 Swedish Crowns, for studies at the University of Colorado, Denver, USA, regarding "technique for studying serum bile acids."

In front of this audience of distinguished nutritionists, I would like to call upon Doctor Olle Hernell and Doctor Antal Nemeth to receive their awards.

Let us now turn to the subject of this symposium. Sensitivity reactions caused by different substances have become an increasing problem. Is there a real increase caused by new substances in our environment, is the population becoming more sensitive, is the increased prevalence merely the result of better diagnosis? If the increase in sensitivity reactions is real, can we do something to stop this development? What can be done to prevent our children from developing sensitivities?

Food sensitivity is one part of this complex problem that is, of course, of special interest to the food industry. There are a number of food

components that traditionally have been connected with food sensitivity. According to Dr. May's findings in the USA, approximately 90 percent of all food sensitivity reactions were caused just by four major foods: nuts, eggs, milk and soy.

Of course, it is essential to individuals who suffer from food sensitivity to be able to get information about the composition of different foods. On prepacked food products the information is usually available in the form of an ingredients list. The sensitive person will then be able to select proper foods—avoidance is often the only cure. The Swedish National Food Administration is well aware of this problem and has made sure that proper information is given. For instance, milk-sugar and proteins from milk, egg, fish, cereals or soy must be declared as such and not hidden under a category name. This Department has even abolished some substances that cause adverse reactions in only a very small group of individuals. This was the case with the azo dyes and "tartrazine," which must not be used in Sweden, unlike most other countries. The definition of the terms "food sensitivity" and "food allergy" has been subject to much discussion. The term "food allergy" has been misused by some to include all kinds of adverse reactions to food. It has been suggested that the term "food sensitivity" should be reserved for reactions caused by immunological mechanisms. But this discussion should be reserved for the symposium. In this symposium, we hope to cover food sensitivity in the broad meaning—immunological, non-immunological as well as psychological reactions. For the food industry it is of vital importance to obtain increased knowledge of food sensitivity and to define what we know and what we do not know.

I am hopeful that this symposium will be as successful as the former ones. I bid you all a most hearty welcome to Marabou. The first speaker will be Dr. Charles May, Professor Emeritus, University of Colorado. We are all anxious to hear his views of food sensitivity—facts and fancies. It is an honor for me to ask you, Professor May, to take the podium and present your paper. □

Food Sensitivity: Facts and Fancies

by Charles D. May, M.D.

The purpose of my presentation is, first, to present the principal *facts* about food sensitivity in simple terms and, second, to discuss some popular *fancies* about reactions to foods which are being promoted in the mass media throughout the world. Let us begin with two questions: What is food sensitivity? Is it the same as food allergy?

Allergy has become a household word and is commonly used to express a person's feeling that unpleasant effects come from his exposure to something which does not harm most people. Almost anything might be blamed, for example, pollens, foods, fumes, smoke and chemicals.

The term allergy was originally introduced into medical science to describe the observation that proteins foreign to the body, such as are contained in pollens, foods and animal sera, which gave rise to no symptoms after their first entrance into the body by inhalation, ingestion or injection, could upon subsequent re-exposure cause impressive reactions. The fundamental aspect of this observation was that a *change* in reactivity had been induced by the first exposure. Over the years, the term allergy came to be applied customarily to an *increase* in reactivity, as in persons who developed hayfever when repeatedly exposed to pollen.

Unfortunately, in connection with reactions to foods, the term allergy has suffered a loss of precise meaning because of erroneous usage by a few physicians holding anecdotal opinions

about reactions to foods. A more descriptive term may be selected if the different types of adverse reactions to foods are considered. The major categories are listed in Table I.

In the biochemical category are found reactions due to deficiencies of digestive enzymes and to toxic substances occurring naturally in foods, such as mushroom poison, or as contaminants and additives. The immunological category contains what would ordinarily be called allergic reactions. In the psychological category are placed adverse reactions related to psychologic disturbances.

Terms commonly encountered in discussions of adverse reactions to food are listed in Table II.

Some agents may be toxic to anyone in the general population, and others may affect only certain individuals for genetic or other reasons, and then the terms idiosyncrasy or intolerance may be applicable. The term *sensitivity*, rather than allergy, may be chosen to designate adverse reactions to foods based on immunologic mechanisms to avoid the confusion created by abuse of the term allergy. These immunologic mechanisms will be explained in a moment.

Questions about food sensitivity apt to come to mind immediately are: What are the manifestations? How prevalent is it? Which foods are most commonly involved? How important is food sensitivity as a cause of illness in various age groups? Can it be prevented?

The answers depend on the criteria adopted for a diagnosis of food sensitivity. What these criteria should be will become apparent in the following brief account of the current concept of food sensitivity based on immunologic mechanisms.

Charles D. May, M.D., is Professor Emeritus, University of Colorado Medical School, Denver, Colorado, USA.

TABLE I

Adverse Reactions to Food

Biochemical

Enzyme deficiency

Toxic substances

Occurring naturally in foods

Contaminants, additives to foods

Immunological

Psychological

Current Concept of Food Sensitivity Based on Immunologic Mechanisms

The essentials of immunologic mechanisms are easy to understand. Without this background, a proper orientation about food sensitivity cannot be achieved. Keep in mind that the fundamental characteristic of immunologic reactions is the *change* in reactivity by foreign substances, which may be either an increase or a decrease in reactivity.

What happens when a foreign substance, for example, a food protein (serving as an antigen) reacts with a cell? After passing through the barrier interposed by the intestinal mucosa, the antigen reaches particular cells, e.g. β -lymphocytes, in the body and stimulates them to produce antibodies. The antigen or the resulting antibody may also alter the reactivity of certain other cells. This sequence of events may result in a state of sensitization.

When a sensitized person eats a food containing protein antigen to which he has become specifically sensitized, certain reactions may occur. The combination of antigen with antibody or of antigen with reactive cell may 1) cause cells of the body to release chemicals

which can mediate various reactions, 2) stimulate cells to produce secretions or to multiply, or 3) cause damage to cells. In the case of antigens which are toxins, such as some bacterial proteins, the antibody may simply neutralize the toxin by combining with it. On the other hand, it may cause sensitivity reactions. The reactions will be recognized clinically by the effects on end organs, for example, on the intestinal tract to produce diarrhea, on the skin to produce hives or on the lungs to cause asthma. If the reactivity to the antigen is *decreased*, we speak of immunity, when *increased*, of sensitivity. Reactions which cause symptoms and signs are called symptomatic, and reactions not detectable by clinical observation are called asymptomatic.

Many details of the chemical structure of antigens and antibodies are known, as well as the types of cells responding to antigenic stimulation and the factors controlling those responses. Many of the complex processes which prevent all but a trace of the huge amounts of antigens contained in our food from crossing the intestinal mucosa have been discovered. Also, considerable progress has been made in explaining why some persons become sensitized by the small amount of antigen that ordinarily does break through this barrier, while most people do not.

Indeed the wonders disclosed by our present knowledge of immunologic reactions to food are as spectacular as the more publicized marvels of astronomy and explorations of space. This will be evident in the presentations and discussions of recent advances by the scientists who will participate in this symposium. Dr. Johansson will review the various types of immunologic mechanisms involved in food sensitivity reactions. Dr. Aas will report on the progress in isolation and purification of antigenic substances in foods. Dr. Metcalfe will consider diagnostic procedures for detection of sensitivity and immunologic reactions. Dr. Foucard will probe the complexity of development of sensitization at various ages and how the process may be prevented. Dr. Bienenstock will describe the regulation of transmission of antigenic materials across the intestinal mucosa. Dr. Anderson is expected to consider the authenticity of certain reactions attributed to

TABLE II

Adverse Reactions to Food

Toxic (Biochemical)

General population

Individuals

Idiosyncrasy

Intolerance

Sensitivity (Immunologic)

food but not shown to be on an immunologic basis.

When such profound understanding of sensitivity to food is now available, it may come as a surprise to learn that there is widespread confusion and controversy about what is commonly called food "allergy." How such confusion and controversy developed will now be traced.

The Emergence of Confusion and Controversy

Charles Richet, Professor of Physiology at the University of Paris, received a Nobel Prize in 1913 for his contributions in the field of allergy. His son, Charles Richet, Jr., working in his father's laboratory, was among the first to study experimental induction of sensitivity to food antigens and was coauthor of a monograph on food sensitivity published in 1919. With this promising start, steady progress through sound clinical and experimental studies might have been expected.

Unfortunately, and perhaps naively, Charles Richet, Jr. joined with Albert Rowe, an American allergist, in publication of a paper in 1930 in the French literature which echoed beliefs Rowe had been proclaiming in the American literature. This paper bore the title "Chronic Nervous Manifestations of Alimentary Anaphylaxis" (anaphylaxis being a type of sensitivity). It contained a collection of sketchy, anecdotal, uncritical case reports of ill-defined neurologic and behavioral disorders, which the authors attributed to "allergy" to food, including headache, migraine, paralysis, epilepsy, neuralgia, itching, dizziness, sleeplessness, drowsiness and aberrations of mental performance and behavior. Publication of this paper bearing the reputable and illustrious name of Richet amounted to opening a Pandora's Box which has not yet been closed. Thereafter many frustrated clinicians seized upon food "allergy" as an explanation of numerous vague and otherwise obscure complaints of their patients.

In the United States, about 1950, Randolph set forth his hypothesis that reactions to foods are commonly based on specific maladaptation to foods in susceptible individuals. Randolph contrived this hypothesis by combining three elements: 1) the diffuse clinical symptomato-

logy of Rowe and Richet just mentioned, 2) an unsupported notion proposed by Rinkel that manifestations of food "allergy" appeared in cycles, one phase being "masked" or without symptoms and 3) a forced analogy with a theory of general adaptation to stress being introduced into physiology by Hans Selye of McGill University at the time.

Although in the subsequent 35 years Randolph's hypothesis has never been subjected to sound scientific evaluation, it has been developed by him and his followers into a system of clinical management of patients rather arbitrarily suspected of adverse reactions to foods. Even though an immunologic basis has been denied, the term "allergy" has been freely used to denote these supposed adverse reactions, with the consequent confusion in meaning of terms and an inevitable controversy with scientific allergists. This Rowe-Rinkel-Randolph School has attracted many followers among physicians and the laity in the United States, has spread to England under the guise of so-called Total Allergy and now is sprouting in Sweden and elsewhere. All these groups march under the alluring banner of Clinical Ecology. It is not unprecedented for promoters of an unorthodox proposal for healing the ill to adopt a title and a vocabulary with deceptive connotations to cloak their activities with nominal acceptability.

A full critique of the views of these Clinical Ecologists cannot be given within the confines of this presentation, but a thorough analysis of their available publications has shown beyond refutation that they have not met the modern requirements for acceptance of a proposal for management of illness. Perhaps the comparison shown in Table III will arouse sufficient skepticism. Here are listed many symptoms of reactions to foods according to Randolph, the prime Clinical Ecologist, in comparison with the symptoms of neuroses tabulated in a recent review article by Marks; the symptoms are identical.

In his earliest writings, Randolph acknowledged a need to distinguish the symptoms he claimed to be reactions to food from the symptoms of neuroses, but neither he nor other Clinical Ecologists have ever made a serious effort to avoid such confusion.

Food (Randolph)

General

Fatigue
Weakness
Sleeplessness
Excess
Urinary

Respiratory

Rapid
Cough

Cardiovascular

Precar
Tachycardia

Neurologic

Poor coordination
Paresis
Dizziness
Headache
Blurred

Behavioral

Anxiety
"Nervous"
Emotional

Gastrointestinal

Nausea
Diarrhea
Abdominal
Bloat
Dry mouth

Musculoskeletal

Myalgia
Numbness
Muscle

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TABLE III

Food (Randolph)	Neurosis (Marks)
General	
Fatigue, unrelieved by rest	+
Weakness	+
Sleep disturbance	+
Excessive sweating	+
Urinary frequency	+
Respiratory	
Rapid breathing	+
Coughing, clearing throat	+
Cardiovascular	
Precardial pain	+
Tachycardia, palpitations	+
Neurologic	
Poor concentration	+
Paresthesias	+
Dizziness, syncope	+
Headache	+
Blurred vision	+
Behavior	
Anxious, irritable	+
"Nervous," apprehensive	+
Emotionally unstable	+
Gastrointestinal	
Nausea, vomiting	+
Diarrhea	+
Abdominal pain	+
Bloating	+
Dry mouth	+
Muscular	
Myalgia	+
Nuchal spasm	+
Muscle cramps	+

In contrast, the findings of scientific studies, particularly with the exclusion of the influence of psychologic influences, have revealed the manifestations of true immunologic sensitivity to food to be those listed in Table IV.

Noteworthy is the absence of the mental aberrations and behavioral disorders so conspicuous in the symptomatology espoused by the Clinical Ecologists.

Now, answers can be attempted to the remaining questions posed earlier in this discussion regarding prevalence of genuine food

TABLE IV

Manifestations of True Food Sensitivity

Signs	Symptoms
Vomiting	Abdominal pain
Diarrhea	Borborygmi
Fatty Stools	Dyspnea
Edema	Itchiness of skin
Rash	Palpitation
Hives	
Eczema	

sensitivity, the most commonly involved foods, the importance as a cause of illness and the possibility of prevention, as understood by scientific physicians.

True sensitivity reactions to foods are most common in infants, the greatest prevalence being among those consuming cow's milk where the incidence may be about 1 in 100. Genuine food sensitivity reactions are relatively uncommon in adults but no satisfactory figure for the prevalence is available.

About 90 percent of food sensitivity reactions are caused by relatively few foods, namely, milk, eggs, nuts, and wheat, but almost any food may give rise to food sensitivity in an occasional individual. In populations with a high incidence of sensitivity to birch pollen, many may also exhibit a cross-sensitivity to certain fresh fruits and vegetables. Some foods have unjustifiably acquired reputations as frequent causes of symptomatic food sensitivity reactions, a notable example being chocolate which is often accused but rarely convicted by scientific evidence.

While sensitivity reactions to foods can be severe and even fatal, this is rare and such a high degree of sensitivity is usually readily recognized so the guilty food can be avoided. Therefore food sensitivity is not a major menace to health, but unjustified diagnoses can result in diets so restricted as to threaten optimal nutrition as well as gustatory pleasure.

Naturally an appealing goal is the development of some means to prevent the acquisition of sensitivity to food in susceptible persons, perhaps through avoidance of common offenders during pregnancy or the early months of

infancy. Such attempts have produced conflicting results and this will undoubtedly be a topic of lively discussion in the symposium tomorrow.

Answers to these questions by Clinical Ecologists would be in sharp contrast because of their fanciful belief that a vast array of symptoms resembling neuroses may be caused by traces of a limitless variety of foods and that as much as 20 percent of the population is so affected. The complicated restrictions of diet, which are imposed to avoid exposure to even fantastically small amounts of foods arbitrarily held responsible for the patient's complaints, may induce malnutrition. That some neurotic persons would be relieved of their complaints through such solicitous and authoritarian attention is to be expected.

One may well wonder how such a difference in opinion concerning reactions to food could exist in modern times. While the scientific view is that sensitivity reactions are based on immunologic mechanisms, Clinical Ecologists

admit they have no idea what causes their hypothetical maladaptation to foods, but certainly an immunologic mechanism is not demonstrable.

Reasons Controversy and Confusion about Reactions to Food Could Develop in Modern Times.

In the not too distant past, physicians made diagnoses of patients' complaints by gazing at a vial of their urine and making a guess as to its contents. (Figure 1)

There was no procedure or body of knowledge then by which the accuracy of the guess could be tested. This did not matter, since any serious illness was treated by the favorite remedy of the times, bleeding by application of leeches or opening a vein. This approach to illness was based on subjective feelings unchecked by objective evaluation.

The present diagnostic skills and numerous effective therapies were acquired largely as the

result of intro illness—the e from objective agnosis, and effective in p These are the tance of any ness. This is t achieved an i reliability in m ure to adhere fic method wil and uncertain

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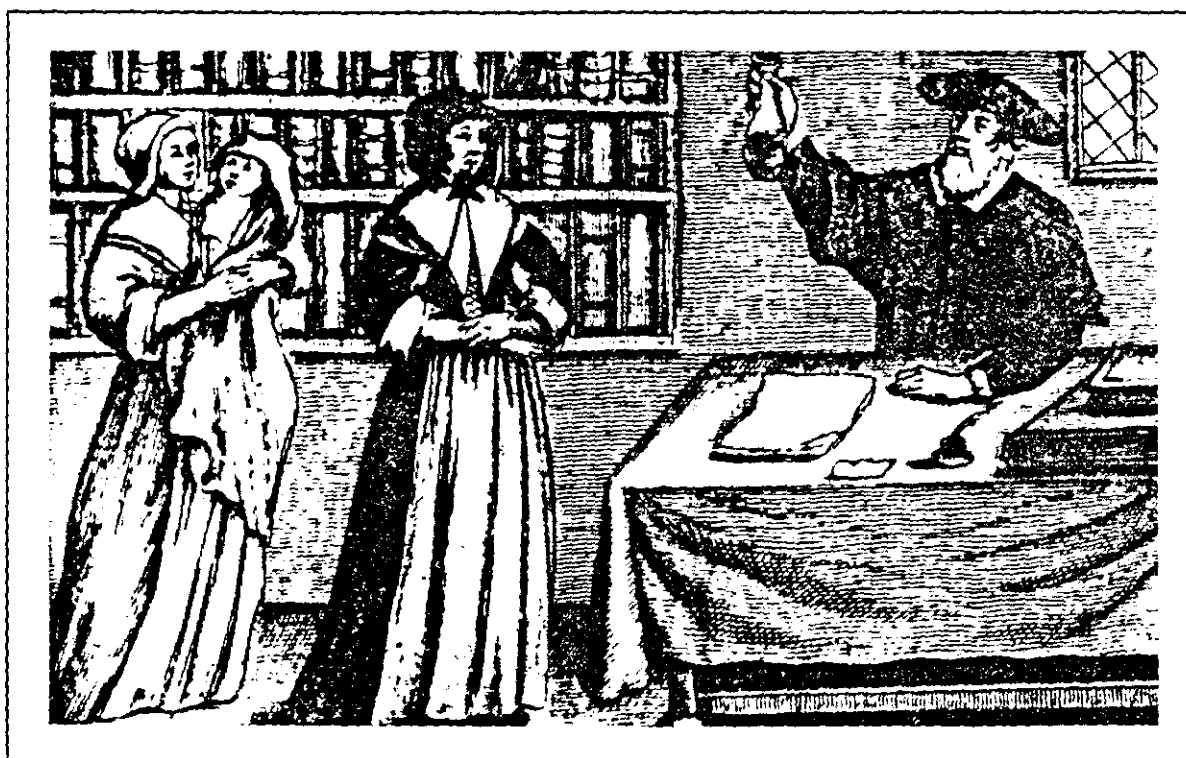


Figure 1: Seventeenth Century Physician (from P. Morel: *The Expert Doctors Dispensary*. London, 1657)

result of introduction of another approach to illness—the employment of sound evidence from objective observations in arriving at a diagnosis, and utilization of therapy shown to be effective in properly conducted clinical trials. These are the modern requirements for acceptance of any proposal for management of illness. This is the scientific approach which has achieved an impressive record of success and reliability in matters of health and illness. Failure to adhere to the requirements of the scientific method will bring a return to the stagnation and uncertainties of the past.

The power of psychologic influences to provoke physical as well as mental symptoms must be appreciated and taken into account if the true origin of many complaints is to be ascertained. Some examples from the scientific literature of the role psychologic influences may play in symptoms mistaken for food sensitivity reactions should prove convincing:

Case 1. Four physician-scientists suffered attacks of migraine they believed to be caused by chocolate, even in minute amounts. Each was given sealed lettered envelopes containing in opaque capsules either 8 grams of chocolate or 8 grams of sugar. The contents were unknown to the observers or the subjects. The capsules were ingested at various intervals during a period of four months. Migraine occurred most commonly without correspondence to ingestion of capsules, and after ingestion of sugar as often as chocolate.

Case 2. A woman had complained for 11 years of symptoms 10 to 20 minutes after swallowing as little as four drops of milk, comprising pressure in the head, blurred vision, dizziness, abdominal cramps, and nausea. (Typical of many patients described by Clinical Ecologists.) An opaque tube was inserted into her stomach through which substances could be injected from behind her so she could not know what was being introduced. When 50 milliliters of milk were introduced, but she was told water was being injected, no symptoms appeared. When 50 milliliters of water were introduced but she was told milk was being given, nausea and abdominal cramps appeared within ten minutes.

Case 3. A man with almost continuous asthma for 17 years which could not be relieved by

epinephrine, an agent usually affording relief in asthma, was given a new drug claimed by a manufacturer to be effective where other drugs had failed. The man experienced complete relief of the long-standing asthma. When all the trial supply had been used, the asthma returned. An additional supply of the drug was requested from the manufacturer and it was then disclosed that the original supply of pills had actually been placebos composed of inert material, furnished to learn whether the new drug truly had a significant effect on asthma.

Numerous such examples of the danger of being misled by subjective observations could be cited, but these should be enough to show the need for proper controls to guarantee that clinical observations are not distorted by psychologic influences.

The best procedure is to administer the suspected food in a double-blind challenge, that is, in a manner that neither the patient nor the observer knows what is being consumed. The suspected food can be given in opaque capsules or hidden in some other food that does not cause reactions.

Without such precautions, the symptoms of a psychoneurosis or an erroneous association of a food with symptoms cannot be reliably distinguished from symptoms due to a physical reaction to a food. In recent scientific studies of persons giving impressive histories of reactions to foods, only about one-third of the histories could be confirmed in blind challenges. This applies to both children and adults.

From the foregoing it is easy to see how Clinical Ecologists can be "successful," even when they do not follow the scientific approach to study of illness. Care should be taken to evaluate patients in such a way that psychologic complaints can be distinguished from physical reactions to foods. Why medical men should forsake their scientific training is an intriguing topic for another lecture. Let us now conclude with the question:

What Can be Done to Help Science Prevail in the Field of Food Sensitivity?

Scientific societies and journals impose strict requirements for acceptance of papers for presentation in meetings or publication to enforce

compliance with the scientific approach to management of illness. Clinical Ecologists must be made to meet the same strict requirements before any papers they may submit for publication in scientific circles are accepted. They must be required to carry the burden of providing scientific proof of their beliefs. Until such proof is forthcoming, their views should be ignored by scientific medical practitioners, thereby avoiding confusion and controversy.

The Clinical Ecologists have made liberal use of the mass media to promote their practices directly to the laity. Scientific professionals can counteract the dissemination of unsound information on matters of health through the mass media by giving their aid to organizations engaged in providing sound guidance to science writers and the public. The American Council on Science and Health, founded by Dr. F.J. Stare and associates, is a shining example. Laymen would do well to turn

to such sources in matters of health, rather than depending on the mass media without question.

The supply of valid information must come from scientific research. This endeavor is greatly facilitated by sponsorship of such conferences as the Marabou International Symposium on Nutrition. Future leaders of scientific research will come from persons trained in Fellowships such as those provided by the Throne-Holst Foundation. Directors of foundations and executives in industry will find support of research is the least costly way to obtain health for the public and prosperity for industry. Unless sound information is available to overpower unfounded claims about reactions to foods, confusion and controversy will surely emerge repeatedly with detrimental impact on the public health, the practice of medicine and the functioning of the food industry. □

Immunology

Dr. G. O. Johansen

The gastrointestinal tract contains 100 to 200 trillion bacteria in the life time of a human. A small selection of these bacteria are valuable substances that are supposed to lead to diseases that are essentially hazardous. enormous loads of these bacteria will result in these symptoms and reactions they

Our knowledge of the mechanisms behind these reactions is difficult to study. Food allergy is such as various often obscure and the application of possible modification place during the production of antigens. We have the technological possibilities of allergy and other types of experimental possible variation in food

The Immune

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